PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 99-499)

In the Application of:	)	
	)	
Chou et al.	)	**Examiner: D. Fox**
	)	
Serial No.: 08/903,944	)	**Group Art Unit: 1638**
	)	
Filing Date: July 31, 1997	)	**Confirmation No.: 3007**
	)	
For: Production of Transgenic Poinsettia	)	

REPLY TO EXAMINER'S ANSWER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The appellants hereby file a reply to the Examiner's Answer in the appeal identified above.

Enablement rejection under 35 U.S.C. § 112, first paragraph

In their opening brief, the appellants cited three Federal Circuit cases for the proposition that composition claims are enabled as long as the specification discloses at least one method by which one of ordinary skill in the art can make and use the claimed composition without undue experimentation: *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1335 (Fed. Cir. 2003); *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998); and *Durel Corp. v. Osram Sylvania Inc.*, 256 F.3d 1298, 1308 (Fed. Cir. 2001). The Examiner answered that these cases are factually distinguishable from the present one. According to the Examiner, while transgenic poinsettia plants made by different methods (e.g., microparticle bombardment vs. *Agrobacterium*-mediated transformation) are not identical, the claimed compositions in the cited cases were identical regardless of the method of producing them. The appellants respectfully disagree—the three cited cases are not distinguishable on this basis.

Of the three cited cases, *Amgen* and *Johns Hopkins* are the most factually similar to this case because, like this case, they both involved inventions in the field of biotechnology. In *Amgen*, the composition claims at issue were directed to a protein, erythropoietin (EPO). In *Johns Hopkins*, the claims at issue were directed to a genus of anti-CD34 antibodies, which are proteins as well. It is widely known that proteins, as complex macromolecules, may exhibit various different primary, secondary, tertiary, and quaternary structures depending on the method by which they are made. For instance, the amino acid sequence of a protein is influenced by post-translational processing, which is influenced by the type of cells in which the protein is made. Although two proteins may have different sequences as a result of such processing, they could, for example, both be considered erythropoietin. Moreover, the cell type in which the protein is made will influence the glycosylation pattern found in the protein. Additionally, the cell type and cell culture conditions will impact the three-dimensional conformation of the protein. All of these factors could affect the activity level of the protein. Therefore, contrary to the Examiner's assertion, the inventions in *Amgen* and *Johns Hopkins* are not identical regardless of the method by which they are made.

Furthermore, the Examiner improperly relied upon an unpublished, uncited opinion in making his assertion that transgenic poinsettia plants produced by *Agrobacterium*-mediated transformation are distinct from those made by microparticle bombardment. *See* Ex. Answer, p. 9. According to the M.P.E.P., § 1208, p. 1200-18 (8th ed., rev. 2, May 2004):

> All correspondence with the Board, whether by the examiner or the appellant, must be on the record. No unpublished decisions which are unavailable to the general public by reason of 35 U.S.C. 122(a) can be cited by the examiner or the appellant except that either the examiner or the appellant has the right to cite an unpublished decision in an application having common ownership with the application on appeal.

The Examiner has acknowledged that the specification is enabling for claims to transgenic poinsettia plants produced by microprojectile-mediated transformation. *See* Final Office Action Mailed 9/26/03 (paper no. 41), p. 2. In both *Amgen* and *Johns Hopkins*, the alleged infringer argued that the claims were not enabled because the specification disclosed only one method of making the claimed compositions. In both cases, the Federal Circuit rejected that argument, stating that the disclosure of merely a single method of making a claimed composition suffices to satisfy the enablement requirement. Under *Amgen*, *Johns Hopkins*, and *Durel*, whether the specification also discloses the produc-

tion of transgenic poinsettia by *Agrobacterium*-mediated transformation or by any other method is irrelevant to the issue of whether the presently pending transgenic plant claims are enabled.

[I think this was too harsh on the Examiner. I think the same thing can be said in a less antagonistic manner.]→Besides incorrectly characterizing the nature of the claimed compositions in *Amgen* and *Johns Hopkins*, the applicants respectfully submit that the Examiner's Answer also mischaracterized *Johns Hopkins* and *Durel*. *Johns Hopkins* was quoted out of context. The Examiner asserted that he "has conclusively demonstrated that the alternative mode of producing the claimed product, namely *Agrobacterium*-mediated transformation, is indeed insufficiently enabled," and therefore the claims in this appeal are not enabled. Ex. Answer, p. 11. However, the full paragraph from *Johns Hopkins* states as follows:

> CellPro finally contends that no one ever succeeded in making CD34 antibodies using either purified My-10+ cells or immuno-precipitated My-10 antigens as the immunogens in the Kohler/Milstein method. Hopkins argues that this fact, even if true, is legally irrelevant because the use of these immunogens was disclosed in the patent specification as alternatives to the preferred use of the KG-1/KG-1a cell line. Hopkins is correct; **CellPro can carry its burden only by showing that all of the disclosed alternative modes are insufficient to enable the claims, because "the enablement requirement is met if the description enables any mode of making and using the invention."** CellPro's silence concerning enablement by use of the KG-1/KG-1a cell lines makes its argument on this point specious.

Johns Hopkins, 152 F.3d at 1361 (emphasis added) (quoting Engel Indus., Inc. v. Lockformer Co., 946 F.2d 1528, 1533 (Fed. Cir. 1991)). As the applicants have enabled making and using the claimed transgenic poinsettia plants by microparticle bombardment (as acknowledged by the Examiner) they have satisfied the enablement requirement pursuant to, *inter alia*, *Johns Hopkins*. **←[Rather than framing the issue in terms of what the examiner would have to show to establish non-enablment, I framed it in terms that the applicant has satisfied the statutory requirements. I don't know why, but I am uncomfortable with it the other way.]**

[Again, too harsh.]→Similarly, the applicants respectfully submit that, contrary to the Examiner's assertion, *Durel* indeed supports their position. While acknowledging that *Durel* stands for the proposition that the enablement of a single method of making a claimed composition is sufficient to enable the composition claim, the Examiner cited a separate portion of *Durel* to support the assertion that *Durel* actually supports the Examiner's position. In particular, the Examiner asserted that "the

Court did not decide that the various types of products encompassed by the claims were all enabled." Ex. Answer, p. 12. **[Aaron, I'm uncomfortable with the following as it seems to me to invite rejection for lack of enablement of the sort you state hasn't yet been questioned. Can you rework this argument in a way that is less suggestive of a basis for rejection?]**→However, that portion of *Durel* is irrelevant here because there is no analogous issue in this case. On the other hand, *Durel* makes it clear that the claimed transgenic poinsettia plants are enabled as long as a single method of making them is enabled:

> We put to rest, however, Sylvania's argument that the patent is not enabled because the inventors failed to prepare coatings from each of the precursors suggested in the specification. If the disclosure enables a person of ordinary skill in the art to make a particular metal oxide coating from at least one of the suggested precursors, the enablement requirement for that oxide coating is satisfied. *See Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998) (stating that the enablement requirement is met if the description enables any mode of making and using the invention). The [district] court's statement that use of some metal precursors would require undue experimentation, even if true, would therefore not be fatal to the validity of the claim if the patent specification enabled the preparation of the particular metal oxide coating asserted to be non-enabled from another precursor of that metal. For example, if the patent specification enabled a person of ordinary skill in the art to make the claimed titanium dioxide coating from a titanium tetrachloride precursor, it would be irrelevant for purposes of validity if the patent specification did not enable its preparation from a titanium isopropoxide precursor.

Durel, 256 F.3d at 1308.

Moreover, the appellants respectfully believe the enablement rejection rests on faulty grounds in the first place. The burden is on the Patent Office to supply scientific evidence or reasoning as to why the claims are not enabled for their full scope:

> As a matter of Patent Office practice, . . . a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented ***must*** be taken as in compliance with the enabling requirement of the first paragraph of § 112 ***unless*** there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.
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> ...
>
> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain ***why*** it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

In re Marzocchi, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). The applicants respectfully submit that the Examiner's Reply does not provide the requisite evidence or reasoning.

The Examiner continues to rely on Follansbee et al., Oran, and Caesar to suggest that *Agrobacterium*-mediated transformation of poinsettia is unpredictable. However, as the appellants argued throughout prosecution, the results published in these references are not predictive of *Agrobacterium tumefaciens*-mediated transformation, as described in the specification at, for example, pages 10-11. The Examiner asserts that Follansbee *et al.* taught that whole *Euphorbia pulcherrima* (poinsettia) cannot be recovered following *A. rhizogenes* transformation. But *Agrobacterium rhizogenes* is not *Agrobacterium tumefaciens*. The difference is significant because *Agrobacterium rhizogenes* systems are designed for obtaining transgenic roots, not whole plants. *Agrobacterium tumefaciens* systems, on the other hand, have been developed to obtain whole plants, such as those presently disclosed. Those skilled in the art would not consider Follansbee *et al.*'s work with *Agrobacterium rhizogenes* indicative or predictive of the likely outcome with *Agrobacterium tumefaciens* systems.

The Examiner further cites Oran and Ceasar in support of the assertion that *Agrobacterium tumefaciens*-mediated transformation is unpredictable and unlikely given the alleged host range limitations of the bacterium and the failure of any workers to report successful transformation of poinsettia via *Agrobacterium tumefaciens*. Oran teaches that an aqueous extract of *Euphorbia peplis* L. inhibited infection of potato tumors by *Agrobacterium tumefaciens*. But *Euphorbia peplis* L. is not *Euphorbia pulcherrima* (poinsettia) as recited in the present claims, and the Examiner has provided no evidence or scientifically valid reasoning that this result with *Euphorbial peplis* L. has any relevance to the ability of *Agrobacterium tumefaciens* to facilitate transformation of *Euphorbia pulcherrima* (poinsettia).

According to the Examiner, Caesar teaches that there are few strains of *Agrobacterium tumefaciens* that successfully infect another *Euphorbia* species, and that no strains were previously reported to be infective. This is not accurate. What Caeser teaches, *inter alia*, is that among the 240 strains of *Agrobacterium tumefaciens* isolated from eastern North Dakota and Montana samples of the noxious weed species leafy spurge (*Euphorbia esula* L.), all 17 pathogenic strains from the Montana sample were pathogenic to leafy spurge and 3 of the 17 pathogenic strains isolated from the North Dakotan leafy spurge sample were pathogenic to leafy spurge. But *Euphorbia esula* L. is not *Euphorbia pulcherrima* (poinsettia) as recited in the present claims, and the Examiner has provided no evidence or

scientifically valid reasoning that this result with *Euphorbial esula* L. has any relevance to the ability of *Agrobacterium tumefaciens* to facilitate transformation of *Euphorbia pulcherrima* (poinsettia).

In summary, the Examiner bases his enablement rejection on teachings of one reference disclosing a different bacterium than recited in the specification and two references disclosing results with different plant species than recited in the present claims. The Examiner fails to provide scientifically supported and acceptable evidence or reasoning why the cited references have any relevance to the present claims. The unstated implication appears to be that the bacterium studied by Follansbee *et al.* and the plant species studied by Oran and Ceasar are of the same genus as the bacterium and plants species (respectively) recited in the present claims and, therefore, one would expect the same results for all members of the genus. The applicants respectfully submit that there is no scientific basis for such an assumption and the Examiner has provided none. Therefore, the Examiner has not met the requirements of *In re Marzocchi*.In view of the foregoing, the appellants respectfully request reversal of the enablement rejection.

Written description rejection under 35 U.S.C. § 112, first paragraph.

The appellants respectfully believe that the Examiner misapprehended their arguments regarding the written description rejection. In contrast to the Examiner's characterization, the appellants did not argue that the written description rejection is improper given the clarification of *Eli Lilly* provided by the Federal Circuit in *Enzo Biochem.* Rather, the appellants argued in their opening brief that *Eli Lilly*, upon which the Examiner heavily and nearly exclusively relies, is not the most relevant case. In *Eli Lilly*, the claims were directed to particular nucleic acids. The issue was whether there was adequate support for claims to a genus of newly discovered nucleic acids when only a small handful of nucleic acid sequences within that genus were disclosed. In stark contrast, the patent application in this appeal does not claim any nucleic acids; rather, it claims transgenic poinsettia plants that express at least one foreign gene. Accordingly, the issue here is whether there is adequate support for claims to such transgenic poinsettia when the written description discloses such transgenic poinsettia plants but does not disclose the sequence of every foreign gene.

The case most relevant to the written description issue in this appeal is *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003). In *Amgen*, the claims at issue were directed

to erythropoietin (EPO) produced by vertebrate (particularly mammalian) cells, as well as processes for producing the EPO from those cells. The issue was whether the written description adequately supported the claim terms "vertebrate cells" and "mammalian cells" when it failed to describe all vertebrate and mammalian cells as engineered in the claimed invention. The court answered that the written description was sufficient:

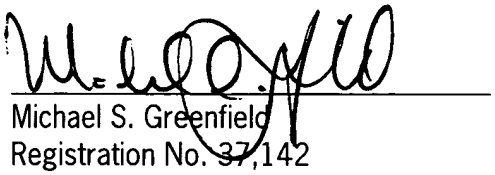
> Both *Eli Lilly* and *Enzo Biochem* are inapposite to this case because the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend. Instead, the claims of Amgen's patents refer to types of cells that can be used to produce recombinant human EPO. Thus, TKT [a defendant] can only challenge the adequacy of disclosure of the vertebrate or mammalian host cell – not the human DNA itself. This difference alone sufficiently distinguishes *Eli Lilly*, because when used, as here, merely to identify types of cells (instead of undescribed, previously unknown DNA sequences), the words "vertebrate" and "mammalian" readily "convey[] distinguishing information concerning [their] identity" such that one of ordinary skill in the art could "visualize or recognize the identity of the members of the genus." *Eli Lilly, 119 F.3d at 1567, 1568.* Indeed, the district court's reasoned conclusion that the specification's description of producing the claimed EPO in two species of vertebrate or mammalian cells adequately supports claims covering EPO made using the genus vertebrate or mammalian cells, renders *Eli Lilly* listless in this case.

Amgen, 314 F.3d at 1332.

The claim terms "vertebrate cells" and "mammalian cells" of *Amgen* are analogous to the claim term "foreign gene" in this case. Just as the Federal Circuit held in *Amgen* that the terms "mammalian cells" and "vertebrate cells" are well known and therefore not new or unknown biological materials that the ordinary skilled artisan would easily misapprehend, "foreign genes" does not describe new or unknown biological materials that the ordinary skilled artisan would easily misapprehend – one skilled in the art can easily apprehend non-poinsettia genes. The appellants respectfully submit that based on the present specification, one of ordinary skill in the art would have no difficulty (a) envisioning a poinsettia plant transformed with a foreign gene, and (b) understanding that the appellants, who for the first time demonstrated success in obtaining whole transformed poinsettia plants, contemplated and had possession of such transformed plants.

In view of the foregoing, the appellants respectfully request reversal of the written description rejection.

Respectfully submitted,



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